
Update on Congenital Cytomegalovirus (cCMV) Diagnosis and Evaluation

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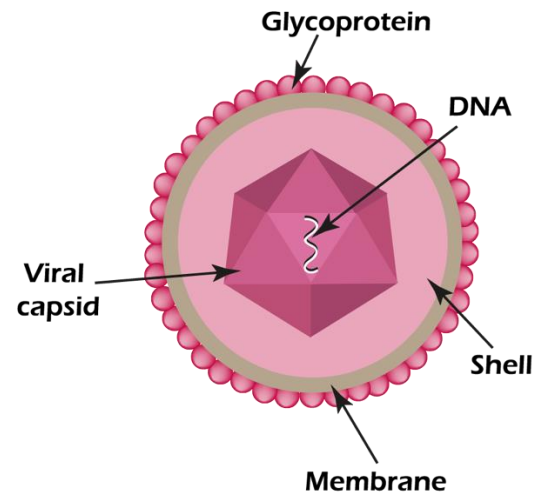
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ValEAR 2 Team

Objectives

The structure of the cytomegalovirus



cCMV and Importance

Diagnosis

Hearing Targeted Testing in 2013

Expanded Targeted Testing in 2019

Comparison to Universal Screening

Our Recommendations

Why cCMV is Important



Courtesy of Kaitlin
Hill and family

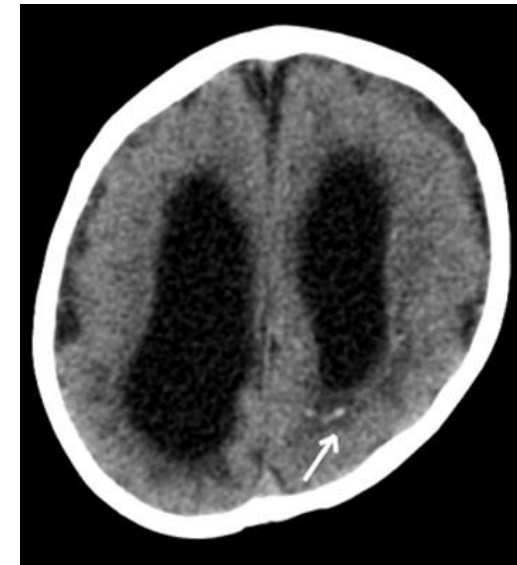
What is Congenital Cytomegalovirus?

- Most common congenital infection worldwide – 0.5% prevalence
- In utero infection
- Important cause of neurodevelopmental delay
- Most common cause of pediatric nonhereditary SNHL (25%)
- Early intervention is important for improving speech and language



CMV Disease

- 10-15% of lab confirmed cCMV positives
- Sensorineural hearing loss
- Abnormal brain imaging, CBC, or transaminases
- Common features: hepatomegaly, splenomegaly, petechiae, IUGR, jaundice, microcephaly, chorioretinitis, SNHL up to 50%



CMV Infection

- 85–90% of lab confirmed cCMV positives
- No symptoms
- Normal imaging, hearing test
- Normal CBC, transaminases
- No treatment consensus



cCMV Diagnosis

- Child less than 2-3 weeks of age
- Postnatal infection not associated with hearing loss
- Urine culture or PCR
- Saliva – breastmilk contamination (26-41% false positive), confirm with urine PCR
- Dried blood spot (DBS) samples



DBS Utility

- Boppana et al: CHIMES March 2007-2008
 - Compared saliva rapid culture to DBS CMV PCR (single and double primer)
 - DBS sensitivity = 34.4%
- Dollard et al. 2021 CDC study on DBS
 - DBS sensitivity 74.2-76.8%
 - Advancements in DNA extraction and PCR amplification have improved performance



Neonatal DBS PCR can be used to retrospectively diagnose the older child

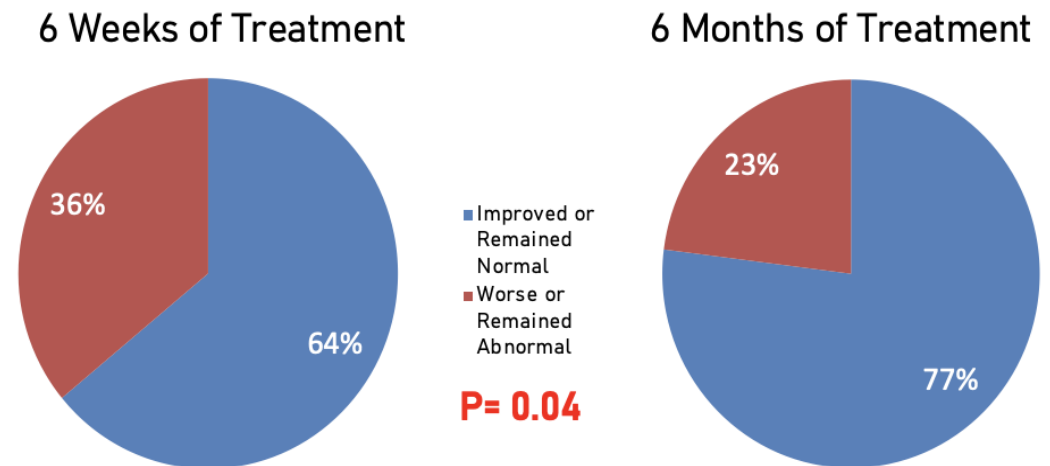
New Information on DBS PCR Testing in Utah

- Zhang et al. study from Utah
 - 79 children underwent DBS testing after 3 weeks of age
 - 19 (24.1 %) positive (oldest child 8 years old) for CMV
 - 7 of 19 (36.8 %) cCMV disease, 4 (21.1 %) cCMV infection, and 8 (42.1 %) cCMV with isolated hearing loss.
- Takeaway: Identified a large number of children over 3 weeks of age

Detect It. Then Treat It?

- Valganciclovir (VGCV) as a treatment for cCMV
 - Not FDA approved for cCMV
- Eligible for early intervention services: get resources, hearing aids, and cochlear implants
- Kimberlin et al: Longer VGCV course improves hearing outcomes up to 2 years after treatment
 - n = 31 (6 weeks) n = 37 (6 months)

Hearing Outcomes



Kimberlin et al. NEJM 2015 PMID 25738669

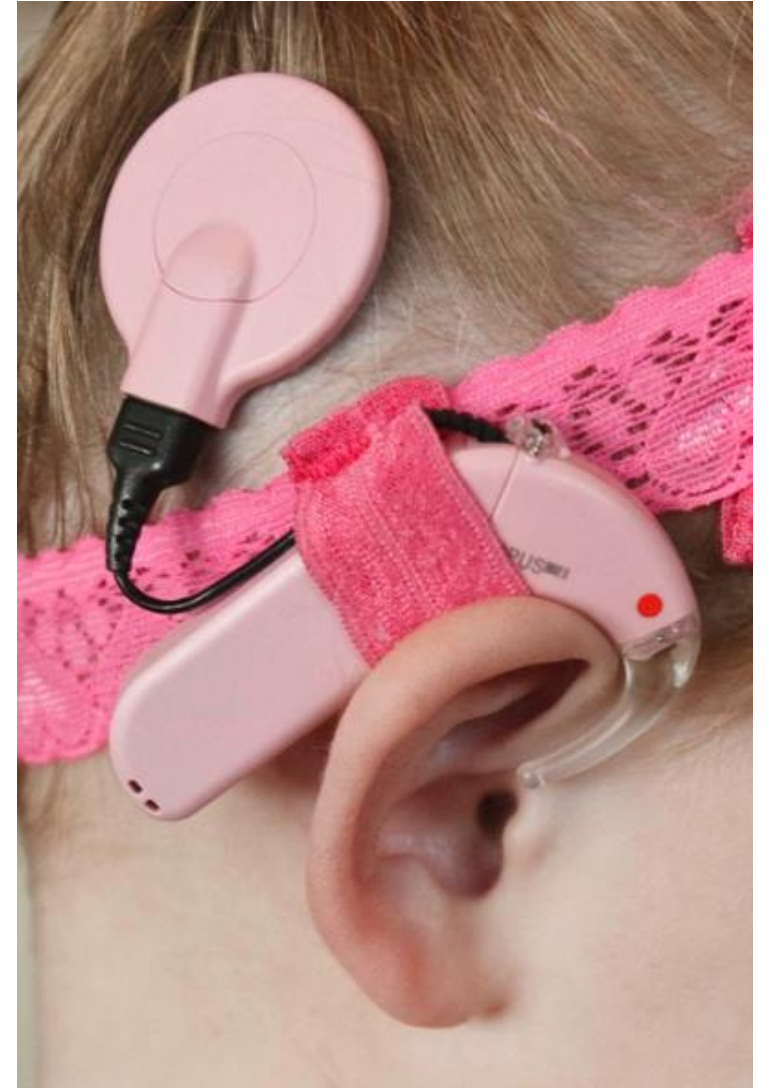
The Story of Daisy

- 19 mo child progressively worsening hearing, Failed NBHS
- U/S findings in utero consistent with cCMV
- Repeat ABR: right profound and left moderate SNHL
- Neonatal Dry Blood Spot CMV PCR- positive
- 6-week course of valganciclovir
- Bilateral cochlear implant
- Utah as a Leader: H.B. 81, July 2013 – Sara Doutre, Ronda Menlove
- DHHS public education program to inform caregivers about CMV
- Test infants < 3 weeks of age for CMV who fail two newborn hearing screening tests and counsel the parents and consider treatment



Hearing Targeted in Utah

- July 1, 2013 – June 30, 2015 – [103,868 births](#)
- 509 never passed NBHS and were eligible for cCMV testing
- 243/509 infants tested for cCMV before 3 weeks of life
 - 14 cCMV positive
 - 6 cCMV disease with SNHL
 - 8 cCMV infection
 - [0.013% prevalence](#)



Expanded Targeted Testing – 2019

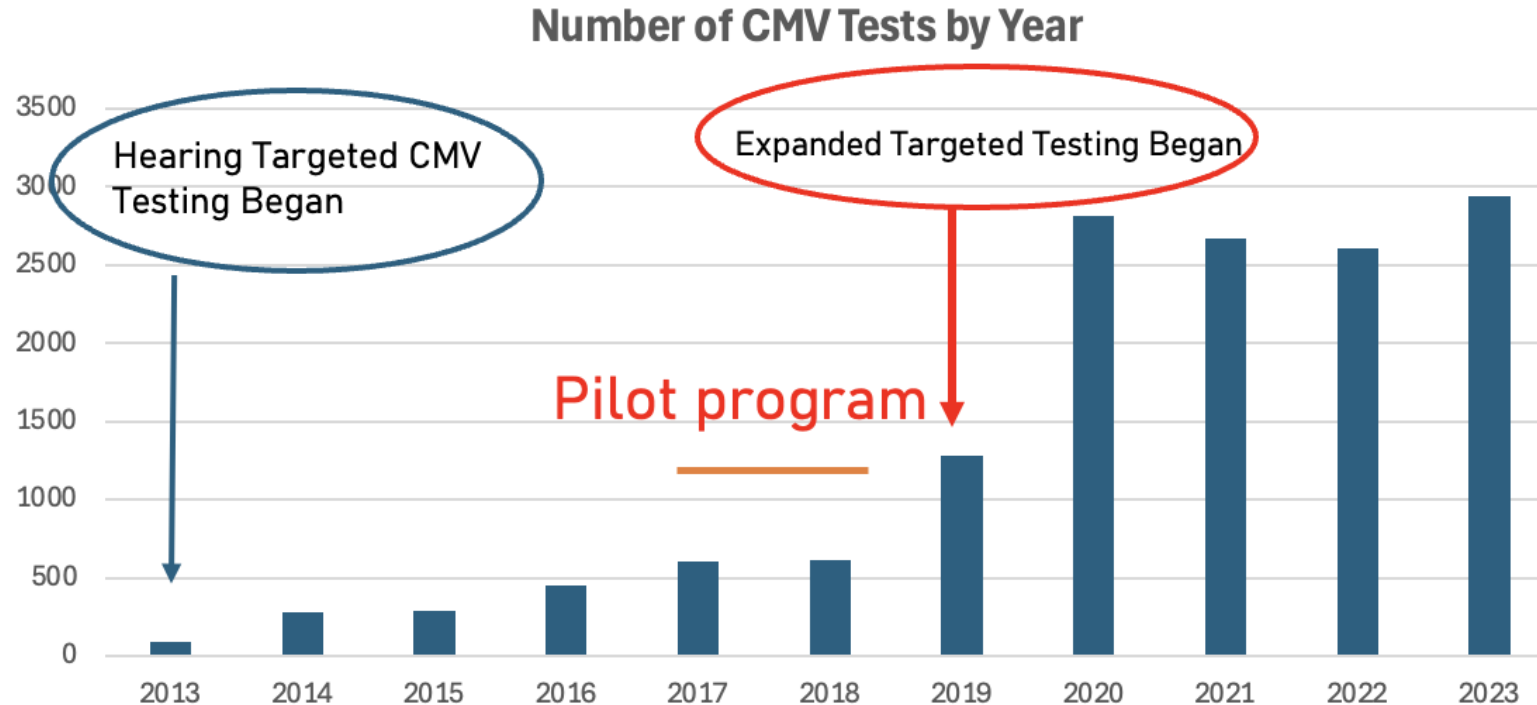
- Improvement on existing program
- Infants with cCMV disease
 - Most at risk for long term sequelae and most likely to benefit from antiviral therapy
- 2024: 69% born at hospitals with expanded testing

If any of the following present:

- | | |
|---|--|
| 1) Mother positive for CMV infection during pregnancy | 7) AST or ALT >100 U/L or unexplained direct bilirubin >1.0 mg/dL |
| 2) Abnormal head size (OFC <10th %ile or >90th %ile at birth) | 8) Petechial rash or blueberry muffin rash at any time |
| 3) Intrauterine growth restriction (weight <10th %ile for gestational age) | 9) Leukomalacia, polymicrogyria, lissencephaly, pachygyria, schizencephaly |
| 4) Unexplained hydrops | 10) Unexplained persistent thrombocytopenia (platelets < 100k/mm3) |
| 5) Intracranial or intraabdominal calcifications on first imaging exam | 11) Failed hearing screen |
| 6) Unexplained hepatomegaly or splenomegaly (>1 cm below the right or left costal margin) | |

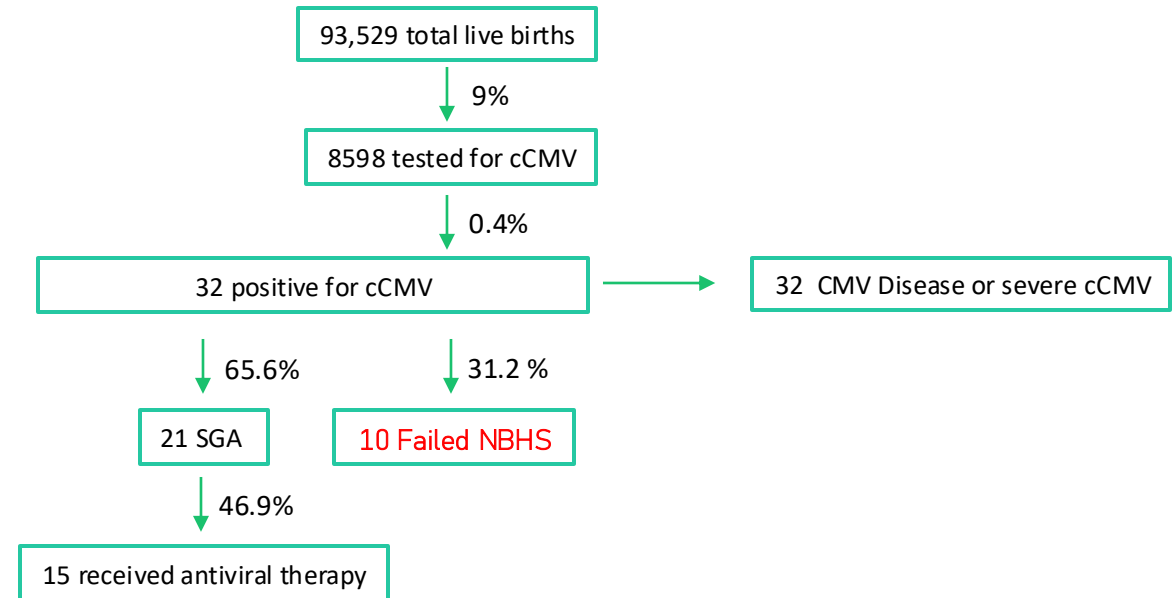
Send urine CMV PCR
(obtain by 21 days of life when possible)

Increase in Testing



Results from March 2, 2021 – August 31, 2024

- Results
 - Higher yield than just from a Hearing Targeted approach (highlighted in red)



Universal vs Expanded Targeted Testing (2019–2023)

Universal DBS:
6 cSNHL per 100,000
births

Expanded Targeted Testing:
10 cSNHL per 100,000
births

Back to Kaitlin Hill





Our Recommendations

- Optimal Approach: Expanded targeted early CMV testing in all Utah hospitals and DBS testing for older patients
 - Identify more treatable cases than hearing targeted alone in an economically feasible manner.
- Other considerations
 - Ensure families are opting in for DBS retention



Questions